**PATENT** 

Attorney Docket No.: JHU1510-2

In re Application of Philip A. Beachy

Application No.: 10/677,982

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## Amendments to the Claims:

Please amend claims 52 and 57 as indicated in the listing of claims.

Please add new claim 58 as presented below.

The listing of claims will replace all prior versions, and listings of claims in the application:

## **Listing of Claims:**

Claims 1 to 51 (canceled)

- 52. (Previously Presented) A method of identifying a compound that <u>modulates</u> phosphorylation of a transcription factor that functions inhibits a phosphatase involved in a hedgehog signaling pathway comprising:
  - a) incubating components comprising the compound, a <u>phosphorylated</u> transcription factor that, when phosphorylated, binds to a hedgehog response element, wherein the hedgehog response element is operatively associated with a target gene, and a phosphatase, under conditions sufficient to allow the components to interact; and
  - b) determining a change in the phosphorylation state of the transcription factor as compared to the phosphorylation state of the transcription factor prior to incubating, measuring the ability of the compound to affect the hedgehog signaling pathway by detecting an increase or decrease in the expression of the target gene wherein a change in the phosphorylation state is indicative of a compound that modulates phosphorylation of a transcription factor that functions in a hedgehog signaling pathway.
- 53. (Previously Presented) The method according to claim 52, wherein the target gene is chloramphenical acetyl transferase.
- 54. (Previously Presented) The method according to claim 52, wherein the target gene is a lacZ gene.

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55. (Previously Presented) The method according to claim 52, wherein the hedgehog response element is a sonic hedgehog response element.

- 56. (Previously Presented) The method of claim 52, wherein the sonic hedgehog response element comprises a nucleic acid having the sequence of SEQ ID NO:1.
- 57. (Currently Amended) The method of claim 52, wherein the transcription factor has been identified by:
  - a) assaying lysate from the cells cultured in media containing an N terminal fragment of a hedgehog polypeptide and identifying as a hedgehog-responsive protein any protein showing induction or increased expression when compared to cells cultured in media not containing the N terminal fragment of a hedgehog polypeptide,
  - b) determining the phosphorylation state of hedgehog-responsive protein identified in step (a) and identifying as a differentially phosphorylated hedgehog-responsive protein any hedgehog-responsive protein that is phosphorylated or dephosphorylated in response to the presence of an N terminal fragment of a hedgehog polypeptide,
  - c) determining whether differentially phosphorylated hedgehog-responsive protein identified in step (d) binds to a hedgehog response element in either its phosphorylated phosphorylated or dephosphorylated state, and
  - d) identifying as a hedgehog-mediated phosphorylation state-dependent transcription factor any differentially phosphorylated hedgehog-responsive protein factor which binds to a hedgehog response element in either its phosphorylated or dephosphorylated state.
- 58. (New) The method of claim 52, wherein the change in phosphorylation state of the transcription factor causes an increase or decrease in expression of the target gene.